PA55

VALIDATION OF A QUANTIFICATION IMAGING SYSTEM FOR THE NORMAL AND OSTEOARTHRITIC KNEE

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Existing methods used to evaluate osteoarthritis (OA) progression, such as cartilage degradation, are imperfect. The aim of our study was to evaluate the reliability of a novel imaging software tool that assesses cartilage volume using magnetic resonance images (MRI) of the knee. The objectives were to assess measurement reliability, i.e. to determine if there are differences between readings of the same image made by the same reader approximately 2 weeks apart (intra-reader variability), if there are differences between the readings of the same image made by different readers (inter-reader variability) and to determine if there are significant differences between the cartilage volume readings obtained from 2 MRI of the knee acquired a few hours apart (test-retest reliability). Forty-eight (48) MRI of the knee from normal subjects, patients with different stages of knee OA, and a subset of duplicate images were systematically and blindly quantified by 3 independent readers using our imaging system. The following cartilage areas were analyzed to compute volume: global cartilage, lateral and medial compartments, lateral and medial femoral condyles.

Reliability of the measurements was assessed using intra class correlation (ICC). For the total cartilage, ICC ranged between 0.986 and 0.995 ($p<0.0001$), for the compartments they ranged between 0.981 and 0.997 ($p<0.000l$) and for condyles between 0.978 and 0.997 ($p<0.0001$). These high ICC values observed indicate high reliability of measurements among the readers. Test-retest data showed excellent consistency with correlation coefficient of 0.99 ($p<0.0001$), and no significant difference between the test and retest visits ($p=0.779$).

These results show that this imaging system is extremely reliable regardless of the reader used and has high test-retest validity. The image acquisition is also highly reproducible. This study represents a first step in the overall validation of an imaging system designed to follow progression of human knee OA and assess disease modifying OA drugs.

PA56

EARLY CARTILAGE DEGENERATION OF THE KNEE AFTER MENISCAL SURGERY: MRI FINDINGS

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Aim: This study examines the prevalence of cartilage abnormalities and the relationship between changes in T2 relaxation times and subsequent cartilage loss in patients at risk of rapid knee cartilage degeneration following meniscal surgery.

Methods: Thirty-five patients (28 men, 7 women) with no radiographic or clinical signs of pre-existing osteoarthritis (OA) who underwent meniscal surgery with or without anterior cruciate ligament repair were examined. MR images were acquired 2 months post-surgery, and yearly for 3 years using a *1.5* T MR scanner and a circumferential knee coil. MRI exams comprised T1-weighted spin echo (SE), T2-weighted fast SE, conventional T1-weighted SE and a fat suppressed spoiled gradient echo (SPGR) sequences. Serial images were subjectively examined side-by-side. We present the results of the first patients to complete the full 3-year evaluation.

Results: Nine cartilage lesions were identified in eight patients, with eight lesions in the femoral cartilage and one in the tibial plateau cartilage. In two patients a high signal focus within the cartilage adjacent to the operated meniscus at baseline progressed to a focal defect within one and two years. One patient had a partial thickness defect that evolved to a full-thickness defect by 1 year. In two other patients, high signal foci in the femoral cartilage persisted on all follow-up exams without progressing to defects. In one patient who had a meniscal repair, a focal high signal lesion visible at baseline disappeared on follow-up examinations and was not associated with any subsequent cartilage loss. In one patient a focal defect appeared at 3 years in the femoral cartilage adjacent to the operated meniscus, without preexisting associated signal abnormalities on earlier examinations. In this same patient a full-thickness of the anterior femoral cartilage appeared 1 year after surgery.

Conclusions: Cartilage degeneration is frequently observed early after meniscal surgery. High signal changes on T2-weighted MRI images seem to precede thickness loss. The results relate most directly to post-traumatic degeneration but are probably applicable also to OA. Larger longitudinal studies are needed, particularly of patients with OA and subjects with risk factors of developing OA, in order to further validate and characterize this intriguing MRI marker of early cartilage degeneration in the knee.

PA57

SPATIAL MRI ASSESSMENT OF ARTICULAR CARTILAGE PROTEOGLYCANS *IN VIVO*

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Aim: Recently, a quantitative MR technique, delayed gadolinium enhanced MR imaging of cartilage (dGEMRIC), has been introduced for the assessment of cartilage proteoglycans (PGs). The technique involves an intravenous administration of the contrast agent Gd-DTPA - which is assumed to distribute into cartilage in an inverse relation to the negative glycosaminoglycans of PGs. Consequently, the T1 relaxation time of the tissue becomes shorter with increasing contrast agent concentration, thus providing a parameter which increases with growing PG concentration. The aim of the present study was to investigate whether this technique could reveal the spatially, from cartilage surface to subchondral bone, varying PG content, known to exist in healthy articular cartilage.

Methods: Patellae of healthy, asymptomatic volunteers (n=6, 3 male and 3 female, age 39+1-11 years), was studied *in vivo* with a clinical 1T MRI system (Siemens Harmony, Erlangen, Germany). Gd-DTPA[2] (0.4ml/kg) was injected intravenously, followed by 10 minutes of knee bending exercises. T1 mapping was performed 2-3 hours after injection in oblique sagittal plane for medial and lateral facets of each patella. An inversion recovery fast spin echo sequence (2mm slice thickness, 0.45*0.45mm pixel size, TE=l5ms, TR=2000ms, T1=25, 100, 200, 400, 600, 1000, l600ms) was used with an imaging time of 17 minutes per slice. For both medial and lateral facets of patellae, spatial Tl -profiles were calculated from cartilage surface to subchondral bone to obtain 5-10 pixels (2.25 - 4.49mm) across cartilage thickness.

Results: T1 relaxation time in the presence of Gd-DTPA[2] ranged from 247 to 524ms among profiles from patellae, with an average value of 355ms. Ten profiles out of twelve revealed an increasing pattern of T1, consistent with the known fact that superficial car-

tilage exhibits lower PG concentration than the deep tissue. Further, in most samples a decrease in T1 near the cartilage-bone interface was observed, also in agreement with the literature on PGs.

Conclusions: The results suggest that changes in the spatial variation of PG concentration may be revealed non-invasively using the present MRI technique. While work on the quantitativeness of the technique is yet necessary, dGEMRIC appears as a promising technique for the assessment of spatial changes in PG content, and is a potential tool for the detection of early OA.

PA58

A NOVEL METHOD FOR FAT SUPPRESSION DURING $T_{1\rho}$-WEIGHTED MRI

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Purpose: To determine the efficacy of a novel method to suppress the contribution from fat/lipid signal during $T_{1\rho}$-weighted MRI.

Introduction: The spin-lattice relaxation time in the rotating frame, or $T_{1\rho}$ provides an alternative contrast mechanism than conventional Tr- and T_2-based MRI methods. This parameter is dependent on the macromolecular environment of the water in the tissue and therefore may be used to map proteoglycan content in articular cartilage. During musculoskeletal imaging however, fat suppression techniques must be employed to increase the contrast between the water-abundant tissues of interest (such as cartilage) and fatty tissue (e.g. bone marrow).

Methods: A three-pulse (90^0-spinlock-90^0) $T_{1\rho}$ pulse cluster was pre-encoded to a conventional 2D fast spin-echo (FSE) imaging sequence. Fat suppression was achieved by setting the length of the spin-locking pulse such that the fat spins are 900 out of phase from the water spins at the end of the pulse. The utility of the pulse sequence was demonstrated by obtaining images of a water and vegetable oil phantom and *in vivo* in the human wrist joint on a 1.5 Tesla GE Signa MR scanner. For comparison, unsuppressed $T_{1\rho}$-weighted images were obtained by setting length of the spin-locking pulse to the time when fat and water spins are in phase. Simulations of the Bloch equations were performed to determine dependence of the fat signal on the imaging parameters.

Results: The images of the phantoms show a marked decrease in the signal intensity of the vegetable oil phantom in the unsuppressed (7600 a.u.) and fat suppressed (1300 a.u.) images while the water signal remained relatively unchanged. The average background signal was 1000 (a.u.) in both images. Employing our technique in imaging the wrist joint significantly reduced the fat signal from the bone marrow in the small bones of the wrist. We confirmed our results with simulations of the Bloch equations for the pulse sequence response.

Conclusion: We have demonstrated the efficacy of a novel pulse sequence to suppress the contribution from the fat/lipid signal in $T_{1\rho}$-weighted MRI. The sequence achieved an additional 80% or more reduction of the overall fat signal compared to the non-suppressed $T_{1\rho}$ image.

PA59

EFFECT OF GLYCOSAMINOGLYCAN DEPLETION ON PROTON $T_{1\rho}$-RELAXATION OF ARTICULAR CARTILAGE

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Purpose: To demonstrate the glycosaminoglycan (GAG) induced changes in $T_{1\rho}$-(spin-lattice relaxation in the rotating frame) dispersion imaging in articular cartilage at 4T.

Methods: $T_{1\rho}$ imaging experiments were performed on a 4 Tesla whole body GE Signa scanner (General Electric Inc., WI). An 11 cm diameter birdcage coil, tuned to 170 MHz, was employed for $T_{1\rho}$ experiments. The pulse sequence used for $T_{1\rho}$ was a Fast Spin Echo (FSE) sequence pre-encoded with a pulse cluster consisting of two hard 90 ^{o} degree pulses separated by a low power rectangle pulse for spin-locking. Fresh bovine patellae were degraded in 0.1mg/ml trypsin solution in phosphate buffered saline (PBS) for a period of 6 hours. $T_{1\rho}$ images were obtained every two hours to monitor the sequential changes in $T_{1\rho}$ relaxation with degradation. $T_{1\rho}$ maps were computed by fitting the intensity of the $T_{1\rho}$-weighted image pixel intensity as a function of length of the spin-lock pulse to an appropriate expression, so that each pixel in the $T_{1\rho}$ map represents a $T_{1\rho}$ relaxation value.

Results: The $T_{1\rho}$ values increased with spin-lock frequency and plateaued between 750-1000 Hz. There is a linear decrease in $T_{1\rho}$ relaxation rate as a function of GAG depletion in cartilage. A higher signal intensity present in the map of the GAG depleted patella was due to the longer $T_{1\rho}$ compared to that of the control patella. Average $T_{1\rho}$ was calculated from several pixels in a region of interest. The $T_{1\rho}$ numbers are highest in the superficial zone and decrease towards the middle zone and again show an increasing trend towards the subchondral bone. This variation in $T_{1\rho}$ seems to closely follow the GAG distribution across the cartilage.

Conclusions: The linear change in $T_{1\rho}$ as a function of percent GAG loss implies that $T_{1\rho}$ imaging can be used to map the GAG distribution in cartilage. As the early osteoarthritic changes are primarily accompanied by the decreased GAG, this technique has potential in measuring and monitoring the early degenerative changes in articular cartilage.

PA60

A METHOD FOR QUANTITATION OF GLYCOSAMINOGLYCAN CONTENT USING PROTON $T_{1\rho}$ IMAGING

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Purpose: To develop a methodology to quantify the absolute glycosaminoglycan (GAG) maps from proton $T_{1\rho}$ (spin-lattice relaxation in the rotating frame) imaging data.

Methods: The methodology was tested on chondroitin sulfate (CS) phantoms and bovine articular cartilage. Seven CS phantoms were made with concentrations of 2,4,6,8,10,15 and 20% in phosphate buffered saline (PBS). Four fresh bovine patellae were depleted with a fresh degradation media containing 0.1mg/ml trypsin in PBS. The amount of GAG depleted from cartilage was measured using dimethyl-methylene blue (DMMB) assay. All the $T_{1\rho}$- weighted images were obtained on a 4 Tesla whole body Signa Scanner (General Electric, WI) using a 10 cm diameter birdcage coil. A series of $T_{1\rho}$-weighted images at different spin-locking length (TSL) were obtained using a fast spin echo pulse sequence pre-encoded with a three pulse spin-lock cluster. $T_{1\rho}$ weighted images were acquired on control patellae before proceeding for degradation. $T_{1\rho}$-relaxation rates were computed by fitting the image data (pixel-by-pixel) to an appropriate theoretical expression.